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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,935	06/08/2001	Hannu T.T. Toivonen	BP101729	8397

466 7590 09/30/2003

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EXAMINER
ZEMAN, MARY K

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,935	TOIVONEN ET AL.	
	Examiner	Art Unit	
	Mary K Zeman	1631	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☒ Claim(s) *1 and 4-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-21 are pending in this application.

Information Disclosure Statement

The references listed on the Information Disclosure Statement of 6/8/01 have been considered, and a copy of the PTO-1449 has been initialed and included with this action. It is noted that this information disclosure statement does not include all the references listed in the specification at page 31. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Further, the reference AJ (Vasko, K 1999) has been considered only to the extent that the examiner understands the language in which it was written. Applicant is encouraged to provide an English language abstract or summary of this reference.

Drawings

The drawings as filed are acceptable to the examiner.

Claim Objections

Claims 1 and 4-8 are objected to because of the following informalities: Each of these claims contain multiple periods. A claim should only have a single period at the end of the claim. The multiple periods are confusing and improper. Alternative ways of separating numerals or step designations include colons or parentheses. [for example "a:" or "a)" instead of "a."] Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The rejected claims are method claims which do not provide a result that is immediately concrete, tangible and useful, as required. The steps of the methods do not lead to a mapped gene as set forth in the preamble, but to a maximized or minimized "score" number, which requires further manipulation, calculation or interpretation. As such, this is insufficient. MPEP 2106: "For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See Alappat, 33 F.3d at 1543, 31USPQ2d at 1556-57 (quoting Diamond v. Diehr, 450 U.S. at 192, 209 USPQ at 10). See also Alappat 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) ("unpatentability of the principle does not defeat patentability of its practical applications") (citing O 'Reilly v. Morse, 56 U.S. (15 How.) at 114-19). A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible and useful. See AT &T, 172 F.3d at 1358, 50 USPQ2d at 1452. Likewise, a machine claim is statutory when the machine, as claimed, produces a concrete, tangible and useful result (as in State Street, 149 F.3d at 1373, 47 USPQ2d at 1601) and/or when a specific machine is being claimed (as in Alappat, 33 F.3d at 1544, 31 USPQ2d at 1557 (in banc)."

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As a whole, claims 1-21 are indefinite as they fail to set forth positive active method steps clearly denoting the steps that are to be performed. For example, in claim 1, step i), "patterns... are searched" is not a positive active recitation. A phrase similar to "searching all marker patterns..." would be a positive active method step.

Further in claim 1, lines 2-4, the metes and bounds of the phrase "which are polymorphic nucleic acid or protein sequences or strings of single nucleotide polymorphisms deriving from a chromosomal region" are unclear. Are both the nucleic acid sequences and protein sequences polymorphic? This is not clear from the wording. It appears "deriving" should be "derived" and it is further unclear how one is to "derive" a SNP from a chromosomal region. A SNP generally has a very specific chromosome and specific chromosomal location with which it is associated.

In claim 1, what is the "chromosome and phenotype data" that is being used? The claim does not require the data to comprise markers or traits- yet the data is supposed to be compared with known marker patterns and predetermined traits. Further, the term "utilizes" lacks description as to how such utilization is to be done. How is the chromosome and phenotype data "utilized" with the marker patterns? How does linkage disequilibrium "utilize" anything? The term "linkage disequilibrium" indicates that two genes or markers are likely to be physically close to one another, as they appear to be "linked" through inheritance studies. It is not a method step or implication of a particular process to be done.

Further in claim 1, step i), what are "all marker patterns" and how are they identified? No marker pattern is previously set forth in the claim such that this limitation is meaningful. The further limitations of "a." do not set forth what the marker patterns are, just that they "involve" genetic markers and their alleles, and perhaps other variables. This is not a definition of a marker pattern, nor is it a method step for creating or determining such a pattern. Further, the substep "b." is indefinite, as it is entirely unclear how a mathematical function "involves some statistical measure of association..." How is it "involved?"

In claim 1 step iii) the steps recited in the claim do not lead to the mapping of any gene. All that is generated is a score that is somehow "based" on maximizing or minimizing an undefined score value. It is not clear how this results in the mapping of a gene.

Regarding claim 1, step iii),, final clause the phrase "as is the case for instance" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 3 recites the limitation "wherein the haplotypes and genotypes referred to in the marker patterns" in reference to claim 1. Claim 1 does not recite the terms haplotypes or genotypes. There is insufficient antecedent basis for this limitation in the claim.

In each of claims 4-8 that recite computer code and input/output definitions, it is unclear what method steps are actually being claimed. While Applicant is permitted to use computer language code in claims, it should be clearly understandable. The metes and bounds of each step must be readily determinable. See MPEP 2106: "When a claim or part of a claim is defined in computer program code, whether in source or object code format, a person of skill in the art must be able to ascertain the metes and bounds of the claimed invention. In certain circumstances, as where self-documenting programming code is employed, use of programming language in a claim would be permissible because such program source code presents "sufficiently high-level language and descriptive identifiers" to make it universally understood to others in the art without the programmer having to insert any comments. See Computer Dictionary 353 (Microsoft Press, 2ed. 1994) for a definition of "self-documenting code."" Applicants are encouraged to functionally define the steps the computer will perform rather than simply reciting source or object code instructions.

Further in each of claims 4-8, it is unclear how the numbering system of the code steps is generated. Each of claims 4-8 separately depend from claim 1, yet the various algorithm steps are consecutively numbered across the claims. If each algorithm must be performed in the order of Claim 4, then Claim 5, then Claim 6, then Claim 7, then Claim 8, (as the numbering scheme suggests) the claims should depend in a chain from claim 1, and not independently from claim 1. The way the claims are written this is not required, making the numbering confusing.

Regarding claims 9-11, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The term "sufficiently reliable" in claims 9, 10 is a relative term which renders the claim indefinite. The term "sufficiently reliable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. When is an estimate sufficiently reliable? How is that determined?.

The term "large enough" in claims 9 and 10 is a relative term which renders the claim indefinite. The term "large enough" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how to determine when the size of S_i is large enough.

It is unclear how the steps of claims 9 and 10 are to modify the method in claim 1. As claim 1 lacks positive active method steps clearly denoting the actions to be taken, it is unclear how the limitations of claims 9 and 10, which are also not positive active method steps, should further limit claim 1.

In claim 11, it is unclear which "p value" in claim 10 is being computed. Claim 10 recites "p value" in at least 3 different places. It is also unclear how this claim modifies the steps set forth in claim 10 or claim 1 from which it ultimately depends.

In claim 12, it is unclear where this limitation should be placed in the method of claim 1. Is it a limitation that occurs at the end of the method? Or is the score refined immediately after being calculated, and before the score is maximized or minimized?

In claim 13, the term "$p(m_i)$" appears to lack antecedent basis in claim 12 and appears to lack basis in claim 1 from which it ultimately depends..

In claim 14, the phrase "the area returned from the prediction of the gene location" completely lacks antecedent basis in claim 1. Claim 1 does not clearly compute an "area returned from the prediction of the gene location." No areas, or locations, or even chromosomes are predicted by following the steps of claim 1.

Claim 15 is not clearly further limiting of claim 1- it appears to repeat limitations already present in claim 1.

Claim 16 is unclear, as it is a run-on sentence that does not clearly set forth the limitations to the method.

The term "sufficiently large" in claim 17 is a relative term which renders the claim indefinite. The term "sufficiently large" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how one would determine when the probability would meet the "sufficiently large" threshold.

urther unclear how claim 17 modifies the method of claim 1.

erm "expert investigation" in claim 18 is a relative term which renders the claim
he term "expert" is not defined by the claim, the specification does not provide a
ascertaining the requisite degree, and one of ordinary skill in the art would not be
pprised of the scope of the invention. It is unclear how one would determine
s investigative powers would be considered at the "expert" level.

urther unclear if "expert investigation" refers only to the marker scores, or whether
tigation" is also required for their visualization.

ntirely unclear how the limitations of claim 19 are to be carried out. There is no
to how to modify the marker patterns to refer to more than one gene. And it would
ne multiple gene process isn't truly "simultaneous" as it is an iterative process.

n 21 is indefinite as it fails to recite elements which would define the computer
only limitations incorporated by the reference to claim 1 are process limitations,
tural limitations. A computer system is an apparatus: the method performed by the
es not define its structure.

Claim Rejections - 35 USC § 102

ollowing is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the
rejections under this section made in this Office action:

on shall be entitled to a patent unless –

nvention was known or used by others in this country, or patented or described in a printed publication in this
eign country, before the invention thereof by the applicant for a patent.

nvention was described in (1) an application for patent, published under section 122(b), by another filed
Jnited States before the invention by the applicant for patent or (2) a patent granted on an application for
by another filed in the United States before the invention by the applicant for patent, except that an
ional application filed under the treaty defined in section 351(a) shall have the effects for purposes of this
ion of an application filed in the United States only if the international application designated the United
nd was published under Article 21(2) of such treaty in the English language.

s 1-21 are rejected under 35 U.S.C. 102(a) as being anticipated by Toivonen et al.

laims are drawn to methods of mapping genes utilizing linkage disequilibrium.
ns of SNP's, or haplotypes or genotypes are searched and evaluated. Each marker

is scored, and the location of the gene is predicted based upon the maximization or minimization of the score.

Toivonen et al. (2000) has a differing inventive entity than the instant application. The reference includes Mathias Herr. Mathias Herr is not an inventor of the instant application. Therefore, this is a proper rejection under 102(a).

Toivonen et al. (AM. J. Hum. Genet: 67:133-145, 2000: PTO-1449 AG) discloses the methods of the rejected claims. This reference discloses computers programmed to carry out gene mapping utilizing linkage disequilibrium. Useful haplotype marker patterns are defined, searched and evaluated. Then each marker is scored, and the gene is localized based upon evaluation of those scores (pages 134-135). The haplotypes can have gaps (see abstract). These methods use programmed computer systems. To the best of the Examiner's ability to differentiate between the claimed algorithms and computer code in claims 4-11 and 15-18, Toivonen et al. appear to discuss each variation (Results and Appendices). The phenotype can be qualitative, such as in a complex disease like Type 1 diabetes (see page 134). The statistical significance of the calculations can be measured against the null hypothesis (page 135) and the phenotypes can be randomly permuted (page 135). The gene location can be contiguous, or a point. Toivonen et al. Assert in the abstract that the method can be extended to include environmental covariates, phenotype measurements, and to find several genes simultaneously. As such, this disclosure meets the limitations of the rejected claims.

Claims 1, 2, 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Threadgill et al. (US 2002/0123058).

Threadgill et al. (US 2002/0123058 A1; having priority to 12/1/2000) discloses methods of gene mapping utilizing linkage disequilibrium. Haplotypes or genotypes are used to identify patterns which are used to search the data, scored, and then used to map the gene of interest. Programmed computers and software are disclosed. As such, this disclosure meets the limitations of the rejected claims.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Pritchard et al. 2001 American Journal of Human Genetics, 69 :1-14. This is a review article discussing the state of the art of linkage disequilibrium studies and genetic mapping at the time of the invention (July 2001).

The following patents or published applications represent the field of gene mapping utilizing haplotypes or genotypes:

Simons (US 5,851,762)

Johnson (US 5,981,832)

Schork (US 2002/0077775)

Schork (US 6,291,182)

Cohen (US 6,537,751).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

The Official fax number for this Art Unit is: (703) 872-9306

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz
9/26/03

MKZ

MARY K. ZEMAN
PRIMARY EXAMINER

AU1631